

## OBSTRUCTIVE PHENOMENA IN VENTRICULAR HYPERTROPHY\*

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The association of muscle hypertrophy in the outflow tract of a ventricle with obstruction to blood flow during systole is being recognized with increasing frequency. This functional stenosis has long been known to appear in the hypertrophied right ventricle following surgical relief of pulmonary valve stenosis (Kirklin *et al.*, 1953; Brock, 1955). It was recognized in the left ventricle by Brock (1957) in patients following aortic valvotomy, and in one during the course of systemic hypertension. In two of the first three patients studied by Morrow and Braunwald (1959), however, there was no apparent cause for the underlying ventricular hypertrophy, resembling in this way that described at autopsy by Teare (1958) as asymmetrical ventricular hypertrophy. Most of the cases described since have been of this type, presenting clinical features of obstruction to left ventricular ejection. In some, associated obstruction has been found in the right ventricle, either in the outflow tract (Morrow and Braunwald, 1959) or lower down in the ventricular cavity (Goodwin *et al.*, 1960).

We have encountered this functional lesion in eight patients over the past two years, associated in all with ventricular hypertrophy of unknown cause. The four cases presented here include one whose signs were purely of right ventricular obstruction, with the lesion wholly localized to that chamber.

### CASE REPORTS

*Case 1.* A 26-year-old woman presented in 1959 with increasing effort dyspnoea over three years. There was no family history of heart disease. The peripheral pulse was normal and the blood pressure was 120/80 mm. Hg. The apex beat was left ventricular. A systolic ejection murmur and thrill were maximal in the second left intercostal space, and a short delayed diastolic murmur was present at the apex. The electrocardiogram showed increased voltage with ST segment depression and T wave inversion in the left ventricular leads. Chest radiographs showed moderate generalized cardiomegaly, without aortic valve calcification.

Cardiac catheterization (Table) showed normal pressures in the right heart. Left ventricular and brachial artery punctures showed a mean pressure gradient during ejection of 71 mm. Hg with a cardiac output of 5.1 l./min. A diagnosis of aortic stenosis was made and operation was performed on June 28, 1960, using cardiopulmonary bypass and anoxic cardiac arrest. Through an incision in the aorta the aortic valve was felt to be normal, with no sub-aortic obstruction. A finger could be passed freely down to the apex. The left ventricular wall was thickened diffusely to about 2.5 cm., with no localized mass. Nothing further was done. After operation she recovered well. There was no apparent change in her condition until her sudden death in June 1962, two years after the operation.

*Comment.* Although localized septal hypertrophy was looked for at operation, there was only diffuse hypertrophy of the left ventricle. Viewed in retrospect, the clinical and haemodynamic findings were

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TABLE  
PRESSURE AND CARDIAC OUTPUT MEASUREMENTS AT REST DURING CARDIAC CATHETERIZATION IN THE FOUR CASES REPORTED

	Case 1	Case 2	Case 3	Case 4
Pressures (mm. Hg)				
Right atrium (mean)	3	4	5	5
Right ventricle (apex)	—	58/2-5	77/2-5	—
Right ventricle (body)	33/0-5	31/0-5	30/2-5	96/0-6
Right ventricle (infundibulum)	—	—	—	18/0-6
Pulmonary artery	30/10	31/16	30/13	18/11
Pulmonary artery wedge (mean)	8	—	—	—
Left atrium (mean)	—	11	13	5
Left ventricle	195/15*	160/5-15	102/8-18	152/2-8
Brachial artery	100/60*	105/66	105/48	168/92
Cardiac output (l./min.)	5.1*	4.5	3.1	5.0

\* Measured under general anaesthesia.

characteristic of functional sub-aortic stenosis, and closely resembled the findings in the first two cases encountered by Morrow and Braunwald (1959). The mode of death two years later suggested a sudden arrhythmia: unfortunately no autopsy was possible.

*Case 2.* A 44-year-old woman presented in 1961 with increasing dyspnoea and syncope on exertion over two months. A brother had died suddenly aged 24 years. On examination the arterial pulse felt normal, with blood pressure 125/80 mm. Hg. The apex beat was left ventricular and displaced almost to the anterior axillary line. A loud ejection systolic murmur was maximal in the fourth left intercostal space. The electrocardiogram showed sinus rhythm with moderate left ventricular hypertrophy and ST segment and T wave abnormalities. The chest radiograph showed left ventricular enlargement with prominent dilatation of the ascending aorta. There was no aortic valve calcification.

Cardiac catheterization (Table) showed an obstructive pressure gradient across the left ventricular outflow tract. The upstrokes of the left ventricular and brachial artery pulses were very notched. The obstruction was greatly increased by intravenous administration of 1 mg. acetyl strophanthidin, the peak pressure gradient increasing from 57 to 113 mm. Hg (Fig. 1). In post-ectopic beats there was a larger obstructive gradient and smaller arterial pulse pressure than in normal beats, both before and after digitalization. There

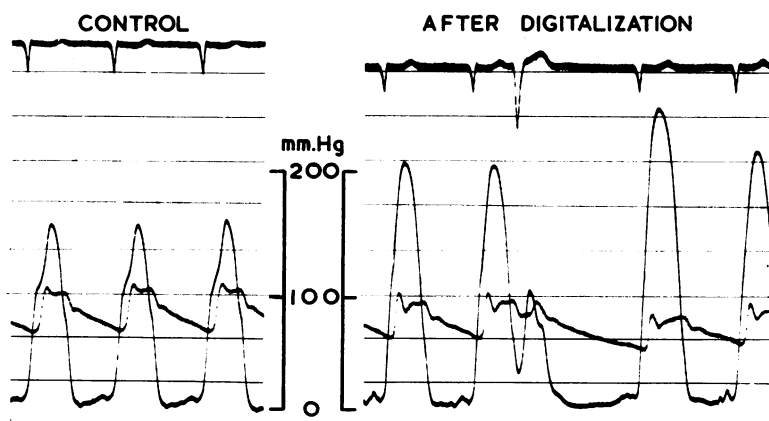


FIG. 1.—Simultaneous left ventricular and brachial arterial pressures from Case 2. The peak pressure gradient was increased from 57 to 113 mm. Hg by 1 mg. intravenous acetyl strophanthidin. Ectopic and post-ectopic beats are shown in the record following digitalization.

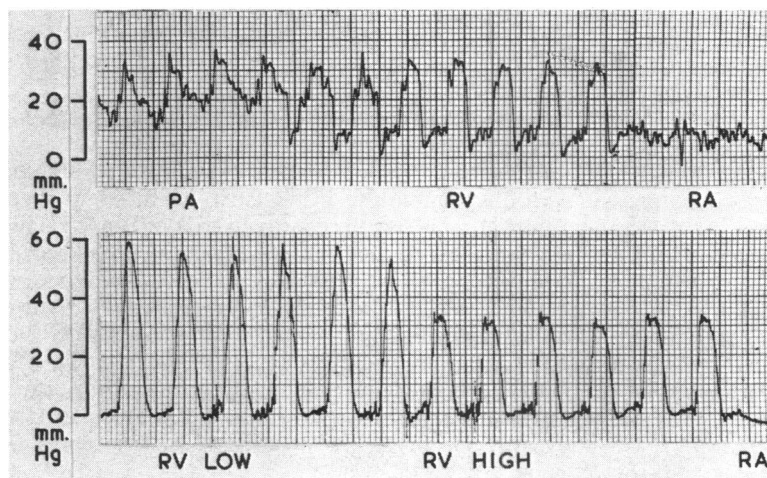


FIG. 2.—Right heart pressures from Case 2. The upper record shows pressures obtained by catheter withdrawal from pulmonary artery to right atrium. The lower record shows withdrawal from the lower half of the right ventricle through upper right ventricle to right atrium. The pressure gradient is not seen during withdrawal from pulmonary artery.

was no diastolic gradient between left atrium and ventricle. In the right ventricle, an obstructive pressure gradient was found, in systole, between the lower and upper halves of the body of the ventricle. The catheter could be withdrawn freely through the upper half of the ventricle from pulmonary artery to right atrium without entering the area of higher pressure (Fig. 2). Selective right ventricular angiography showed a filling defect in the lower half of the ventricular cavity, arising from the hypertrophied interventricular septum (Fig. 3).

In view of her severe symptoms, it was decided to attempt resection of the obstructing muscle in the left ventricle, using the method suggested by Cleland (Goodwin *et al.*, 1960). At operation gross septal hypertrophy was found, presenting the picture of a tumour-like mass bulging anteriorly and into both ventricles. There was also considerable generalized left ventricular hypertrophy. Cardiopulmonary bypass was established, and blood temperature was reduced to 23°C. Through an aortic incision the septal mass could be felt 2 cm. below the aortic valve. The endocardial surface of the mass was incised from above downwards and muscle was resected to establish a channel down to the cavity of the ventricle. The right side of the septum was not touched. From the resumption of sinus rhythm, the electrocardiogram showed left bundle-branch block.

Her immediate post-operative recovery was slow with hypotension, and was complicated by lung collapse. After five days she developed congestive heart failure which proved refractory to the usual treatment, except that she seemed worse when



FIG. 3.—Selective right ventricular angiogram from Case 2 showing a filling defect involving the right ventricular cavity. This was associated with gross hypertrophy of the interventricular septum.

digoxin was suspended for a week. First degree heart block, atrial tachycardia, and atrio-ventricular dissociation appeared in succession over subsequent weeks. The cardiac output remained low, and chest radiographs showed enormous cardiac dilatation. She gradually weakened and died nine weeks after operation. No autopsy was performed.

Microscopic examination of the tissue removed from the septum showed hypertrophied muscle fibres. The arrangement of muscle bundles was somewhat irregular.

*Comment.* Localization of the hypertrophied muscle was the striking feature in this case. Functional sub-aortic obstruction was present, with obstruction also in the cavity of the right ventricle. The poor result obtained by resection was anticipated after finding the enormous bulk of abnormal tissue at operation.

*Case 3.* A woman now aged 53 presented first in 1960. A systolic murmur had been heard at 26 years of age. She had been asymptomatic until aged 40, when she developed dizzy episodes with rapid palpitation. These lasted some five minutes and were increasing slowly in frequency. Their exact nature was never established. One brother who died suddenly aged 41 had several 'black-outs' in the year before death. On examination the pulse was normal, and blood pressure was 140/90 mm. Hg. The apex beat was left ventricular. There was an ejection systolic murmur equally well heard in the aortic area, left sternal edge, and at the apex. The electrocardiogram showed sinus rhythm with PR interval 0.12 sec., considerable left ventricular hypertrophy, an intraventricular conduction delay, and ST segment and T wave abnormalities. Chest radiographs showed moderate cardiomegaly.

The dizzy spells were thought to be associated with an arrhythmia, and she was given quinidine, increasing to a dose of 18 grains a day. Over the next two years the episodes were less frequent. No further symptoms have developed, but it was decided recently to clarify the diagnosis by cardiac catheterization. This was performed without change in quinidine therapy. Left heart pressures showed no evidence of obstruction in normal beats (Table). However, a small systolic pressure gradient up to 17 mm. Hg was found between the left ventricle and brachial artery in beats following a long post-ectopic pause. In the right ventricle, a distinct pressure gradient was found between the lower third and upper part of the chamber.

*Comment.* The clinical picture in this patient is of left ventricular hypertrophy, and a diagnosis of functional sub-aortic stenosis was made before catheterization. Little if any evidence for this was found. It is possible that quinidine therapy inhibited the functional obstruction: certainly this drug has given her symptomatic relief.

*Case 4.* A 17-year-old girl had a heart murmur detected at 3 years of age. She had been easily tired through childhood, and was slightly limited on exertion by dyspnoea. The family background was unknown. The positive signs were a slight right ventricular lift, and a systolic thrill and ejection murmur maximal in the third left intercostal space with a normal pulmonary valve closure sound. The electrocardiogram showed a 3 mm. R wave with 1 mm. S wave and upright T wave in V1. It was otherwise normal. The chest radiograph was normal. A diagnosis of infundibular pulmonary stenosis was made and this was confirmed by cardiac catheterization (Table). The left heart pressures were normal.

An operation was undertaken with cardiopulmonary bypass. A solid tumour-like mass of tissue was found to occupy the anterior wall of the right ventricular outflow tract and the upper third of the right ventricle. Although somewhat paler than normal, the mass merged gradually into the surrounding muscle, and it appeared to contract normally. The remainder of the right ventricle was a little hypertrophied; the left ventricle was normal. Through the right atrium the mass was felt to compress the outflow tract in systole and extended to within 1 cm. of the pulmonary valve. The obstructing tissue was resected through a ventriculotomy. No pressure gradient was present at the conclusion of the operation.

Recovery was uncomplicated. In the year since operation she has been very well, and notices an increase in effort tolerance. The electrocardiogram shows an incomplete right bundle-branch block.

Microscopic examination of the resected tissue showed interlacing bundles of very large muscle fibres, separated by considerable connective tissue (Fig. 4).

## DISCUSSION

The various sites at which functional obstruction has been found in ventricular hypertrophy are all shown in the cases reported, occurring either alone or in combination. Although usually asymmetrical, the hypertrophy may be diffuse, as in Case 1, and in cases confirmed at autopsy by Bercu *et al.* (1958) and by Paré *et al.* (1961). Localization purely to the right ventricle, as in our Case 4, has not previously been shown.

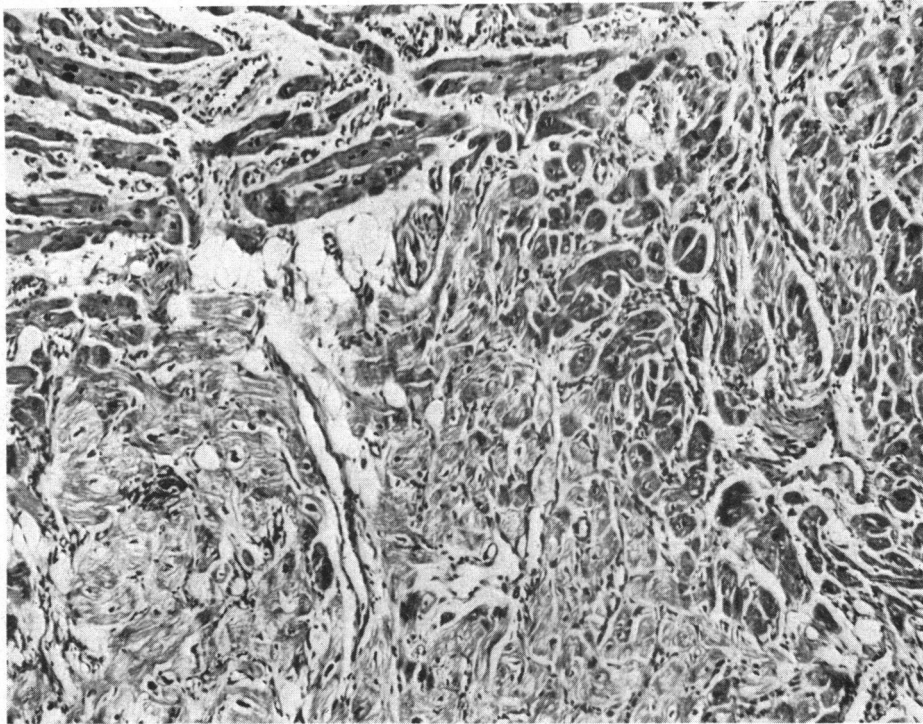


FIG. 4.—Photomicrograph of heart muscle from Case 4 showing bundles of large muscle fibres separated by considerable connective tissue ( $\times 100$ ).

All cases with functional obstruction have in common ventricular hypertrophy which is out of proportion to the existing pressure load on the ventricle. This is so whether the hypertrophy developed without known cause or was secondary to valve stenosis, or whether it was localized or diffuse. The severity of the obstruction is consistently dependent on myocardial contractility as has been emphasized by the studies of Braunwald and his colleagues (Brockenbrough, Braunwald, and Morrow, 1961; Braunwald, Brockenbrough, and Frye, 1962) and as was shown by digitalization in our Case 2. These facts suggest that localized muscle bulk is not important in producing anatomical obstruction. They rather suggest that obstruction is a result of unbalanced and abnormal contraction of the outflow tract.

For similar reasons we would not expect the hypertrophied muscle to present a localized obstruction to ventricular filling in diastole. None of our patients has shown a pressure gradient between atrium and ventricle to suggest this, nor has this been reported from elsewhere. Clinical evidence for obstruction to ventricular filling, as described by Goodwin *et al.* (1960), can be explained by a generalized reduction in distensibility of the hypertrophied ventricle. With this reasoning a slightly different emphasis may be given to the treatment of functional obstruction. Excision of muscle bulk *per se* seems of minor importance, except as one means of reducing the contractile power of the infundibulum. It is possible that simple incision may in some cases be as effective and less dangerous than more extensive excision. It is even possible that the same effect might be obtained by careful use of cardioplegic drugs, and in this regard the findings during quinidine therapy in our Case 3 are of interest. Haemodynamic as well as clinical assessment of such therapy would be valuable.

## SUMMARY

Four selected cases are presented as examples of functional obstructive phenomena caused by ventricular hypertrophy. They include one example not previously reported, where the disease was restricted to the right ventricle. Emphasis is placed on the functional nature of the obstructive lesions and the importance of this in deciding on any definitive treatment.

The operations described were performed by Mr. R. Nicks (Cases 1 and 4) and Mr. A. F. Grant (Case 2). We are grateful to Eli Lilly and Co., Indianapolis for supply of acetyl strophanthidin.

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